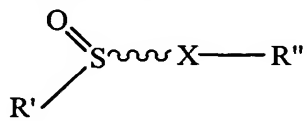


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CLAIMS

1. A process for preparation of a sulfoxide compound that is substantially optically pure or optically enriched, said process comprising:

a) providing, in an organic solvent, a starting material that is a mixture of optical isomers of the sulfoxide group-containing compound of the structure



or a salt thereof, said different optical isomers having R and S configurations at the sulfur atom of the sulfoxide group;

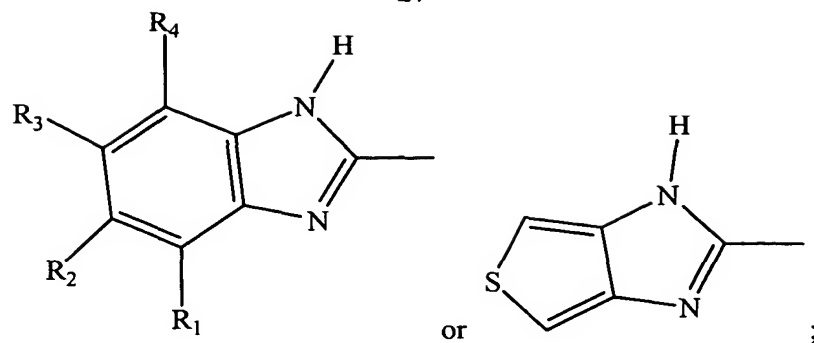
b) reacting said mixture of optical isomers, in said organic solvent, with i) a coordinating agent containing a transition metal, and ii) a chelating agent, thereby each of said optical isomers forms a transition metal complex therewith at said sulfoxide group;

c) reacting said mixture of transition metal complexes with an organic acid, or a salt thereof, which is capable of forming an addition product with said transition metal complex; wherein at least one of said chelating agent and said organic acid contains a chiral center and is in a substantially enantiomerically pure form with respect thereto; thereby each of said transition metal complexes of said optical isomers forms an adduct with said organic acid or a salt thereof, said different adducts having at least one physical property in which they differ from one another;

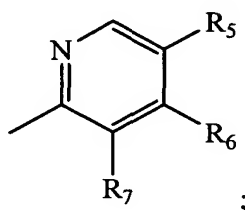
d) separating one of said adducts from the other adduct based on said at least one different physical property;

treating said separated adduct with an external acid or base to decompose said transition metal complexation at said sulfoxide group, thereby obtaining a product, which is one of said optical isomers of said sulfoxide compound in a substantially optically pure or optically enriched form;

wherein R' is

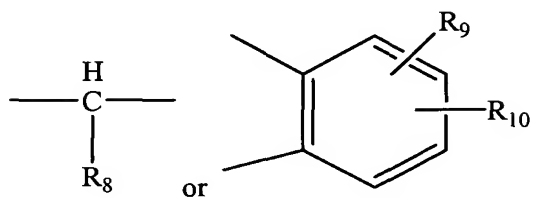


R'' is



and

X is



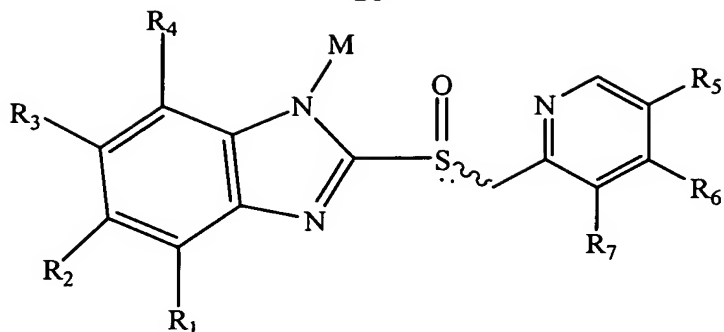
where R₁, R₂, R₃, and R₄, which may be the same or different, are each independently hydrogen, alkyl, alkoxy, halogen, halogenated alkoxy, alkylcarbonyl, alkoxy carbonyl, oxazolyl, or trifluoroalkyl;

R₅, R₆, and R₇, which may be the same or different, are each independently hydrogen, alkyl, halogenated alkyl, alkylthio, halogenated alkylthio, alkoxy, halogenated alkoxy, alkoxyalkoxy, dialkylamino, piperdino, morpholino, halogen, phenylalkyl or phenylalkoxy;

R₈ is hydrogen or lower alkyl;

R₉ and R₁₀, which may be the same or different, are each independently hydrogen, halogen, alkyl or alkoxy.

2. The process of claim 1, wherein said starting material is a salt of the structure:



wherein M is an alkaline metal.

3. The process of claim 2, wherein M is sodium.
4. The process of claim 2, wherein R₁, R₂, R₃, and R₄ are hydrogen.
5. The process of claim 4, wherein R₅ is hydrogen and R₇ is methyl.
6. The process of claim 5, wherein R₆ is -O(CH₂)₃OCH₃.
7. The process of claim 5, wherein R₆ is -OCH₂CF₃.
8. The process of claim 2, wherein R₁, R₃, and R₄ are hydrogen; R₂ and R₆ are methoxy; and R₅ and R₇ are methyl.
9. The process of claim 2, wherein R₁, R₃, R₄, and R₅ are hydrogen; R₂ is difluoromethoxy; and R₆ and R₇ are methoxy.
10. The process of claim 2, wherein said step of providing the starting material comprises suspending said salt in said organic solvent.
11. The process of claim 10, wherein said step of forming a transition metal complex further comprises reacting said starting material with said coordinating agent and said chelating agent in a presence of an organic base.
12. The process of claim 1, wherein said at least one different physical property is solubility of said adducts in said organic solvent.
13. The process of claim 12, wherein said step of separating said adducts comprises precipitating the less soluble adduct under conditions in which the more soluble adduct remains substantially in solution.
14. The process of claim 13, wherein said step of treating said less soluble adduct comprises suspending said less soluble adduct in an aqueous/organic solvent mixture under acidic or basic conditions.
15. The process of claim 14, wherein said step of treating said less soluble adduct comprises reacting with sodium bicarbonate.
16. The process of claim 12, further comprising decomposing said transition metal complexation of said more soluble adduct to obtain a second optical isomer of said

sulfoxide compound different from said first isomer obtained from the less soluble adduct.

17. The process of claim 16, further comprising racemizing said second optical isomer to obtain a mixture of different optical isomers having R and S configurations at the sulphur atom of the sulfoxide group.

18. The process of claim 1, wherein said organic solvent is a ketone, an ester of an organic acid, a nitrile, or mixture thereof.

19. The process of claim 1, wherein the organic solvent is acetone, ethyl acetate, acetonitrile, or mixture thereof.

20. The process of claim 1, wherein said chelating agent is diethyl tartrate.

21. The process of claim 11, wherein said organic base is an organic amine base.

22. The process of claims 21, wherein said organic amine base is di-isopropyl ethyl amine, tri-ethyl amine, or mixture thereof.

23. The process of claim 1, wherein said coordinating agent is titanium (IV) isopropoxide.

24. The process of claim 1, wherein said organic acid is L-mandelic acid.

25. The process of claim 1, wherein said organic acid is D-mandelic acid.

26. The process of claim 10, wherein the organic solvent is an alkyl ketone.

27. The process of claim 26, wherein said alkyl ketone solvent is selected from the group consisting of acetone, ethyl methyl ketone, methyl isobutyl ketone, diethyl ketone, or mixtures thereof.

28. The process of claim 26, wherein said alkyl ketone solvent is acetone.

29. The process of claim 1, wherein the organic acid or salt thereof is added while stirring for about 15 minutes to about 5 hours at about ambient temperature.

30. The process of claim 14, wherein said aqueous/organic solvent mixture includes organic solvents selected from the group consisting of chloroform, dichloromethane, dichloroethane, carbon tetrachloride, or mixtures thereof.

31. The process of claim 30, wherein said aqueous/organic solvent mixture includes dichloromethane.

32. The process of claim 1, wherein said separation step comprises filtration.

33. The process of claim 1, further comprising converting the optical isomer obtained from one of the adducts into its salt form.

34. The process of claim 33, wherein the salt of said one of said optical isomers of said sulfoxide compound, in a substantially optically pure or optically enriched form, is an alkaline salt or alkaline earth salt.
35. The process of claim 33, wherein the salt of said one of said optical isomers of said sulfoxide compound, in a substantially optically pure or optically enriched form, is salt of magnesium, sodium, or potassium, or hydrates thereof.
36. The process of claim 1, wherein said starting material is omeprazole.
37. The process of claim 36, wherein said chiral organic acid is L mandelic acid.
38. The process of claim 37, wherein said chelating agent is diethyl D tartrate.
39. The process of claim 36, wherein said chiral organic acid is D mandelic acid.
40. The process of claim 37, wherein said chelating agent is diethyl L tartrate.
41. The process of claim 36, wherein said product is an R enantiomer of omeprazole.
42. The process of claim 36, wherein said product is an S enantiomer of omeprazole.
43. The process of claim 41, wherein said R enantiomer of omeprazole has optical purity greater than about 99.7%.
44. A process of separating the enantiomers of omeprazole, said process comprising:
- providing a suspension of a salt of omeprazole in an alkyl ketone solvent;
 - reacting said salt of omeprazole with titanium (IV) isopropoxide and diethyl D-tartrate in the presence of an organic base;
 - reacting the product of said reaction with L mandelic acid;
 - maintaining the reaction mixture until a solid mass separates;
 - wherein said solid mass being a mandelic acid salt of a titanium complex of the S enantiomer of omeprazole.
45. The process of claim 44, further comprising filtering said solid mass.
46. The process of claim 45, further comprising reacting said mandelic acid salt with an aqueous base thereby obtaining a residue, which is a free species of esomeprazole.

47. The process of claim 45, further comprising re-precipitating said residue from a mixture of water and acetone to obtain a solid that is an amorphous form of free species of esomeprazole.
48. The process of claim 45, further comprising reacting said free species of omeprazole with a magnesium metal in the presence of dichloromethane in an alcoholic solvent thereby obtaining a residue of magnesium salt of esomeprazole.
49. A magnesium salt of esomeprazole produced by the process of claim 48.
50. The process of claim 48, further comprising dissolving said residue of magnesium salt of esomeprazole in acetone and lowering the temperature of said acetone solution to cause the magnesium salt of esomeprazole to precipitate therefrom.
51. A magnesium salt of esomeprazole produced by the process of claim 50.
52. The process of claim 48, wherein said alcoholic solvent is methanol.
53. The process of claim 45, wherein said ketone is acetone.
54. The process of claim 45, wherein said organic base is di-isopropyl ethyl amine, triethyl amine, or mixture thereof.
55. The process of claim 46, wherein said aqueous base is a solution of sodium bicarbonate in water.
56. The process of claim 55, wherein said sodium bicarbonate is present in said solution at a concentration of about 5% by weight.
57. A compound which the amorphous esomeprazole produced by the process of claim 47.
58. A pharmaceutical composition comprising i) the amorphous esomeprazole produced by the process of claim 47; and ii) one or more pharmaceutically-acceptable excipients.
59. The pharmaceutical composition of claim 58, which is a solid dosage form for oral administration.
60. The pharmaceutical composition of claim 59, wherein said solid dosage form is a tablet.
61. A method of preventing or treating undesirable gastric acid secretion or stomach ulcers, comprising administering to a subject in need thereof a pharmaceutical composition containing an effective amount of the amorphous esomeprazole produced by the process of claim 47.
62. The method of claim 61, wherein said pharmaceutical composition is intended for oral administration.

63. The method of claim 62, wherein said pharmaceutical composition is a suspension, a solution, a powder, a tablet, or a capsule.